Original article

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Occupation, pesticide exposure and risk of multiple myeloma

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Objectives This population-based case-control study examined the relationship between occupation, living or working on a farm, pesticide exposure, and the risk of multiple myeloma.

Methods The study included 573 persons newly diagnosed with myeloma and 2131 controls. Information was obtained on sociodemographic factors, occupational history, and history of living and working on a farm. Occupational and industrial titles were coded by standardized classification systems. A job-exposure matrix was developed for occupational pesticide exposure. Odds ratios (OR) and 95% confidence intervals (95% CI) were estimated by unconditional logistic regression.

Results Farmers and farm workers had odds ratios of 1.9 (95% CI 0.8–4.6) and 1.4 (95% CI 0.8–2.3), respectively. An odds ratio of 1.7 (95% CI 1.0–2.7) was observed for sheep farm residents or workers, whereas no increased risks were found for cattle, beef, pig, or chicken farm residents or workers. A modestly increased risk was observed for pesticides (OR 1.3, 95% CI 0.9–1.8). Significantly increased risks were found for pharmacists, dieticians and therapists (OR 6.1, 95% CI 1.7–22.5), service occupations (OR 1.3, 95% CI 1.02–1.7), roofers (OR 3.3, 95% CI 1.1–9.8), precision printing occupations (OR 10.1, 95% CI 1.03–99.8), heating equipment operators (OR 4.7, 95% CI 1.4–15.8), and hand molders and casters (OR 3.0, 95% CI 1.0–8.4).

Conclusions A modest increased risk of multiple myeloma is suggested for occupational pesticide exposure. The increased risk for sheep farm residents or workers indicates that certain animal viruses may be involved in myeloma risk.

Key terms case-control study, job-exposure matrix, multiple myeloma, occupation, pesticides.

In the United States, the annual age-adjusted incidence and mortality rates for multiple myeloma rose sharply from the 1950s to the 1980s and then leveled off, with rates twofold higher among blacks than whites (1, 2). The causes of multiple myeloma, the reasons for the rise, subsequent stabilization of rates, and the racial disparity in rates are unclear (3).

Although agricultural and farming occupations, including those with exposure to pesticides and farm animals, have previously been linked with multiple myeloma in numerous epidemiologic studies (4–7), most of the epidemiologic studies did not include detailed exposure assessments. These studies were based on an analysis by occupational title, although a few studies evaluated the use of specific pesticides (6, 8). In this paper, we have utilized data from a large population-based case-control study of multiple myeloma among blacks and whites in the United States (US) to investigate the role

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of occupation, including history of living on a farm, and to further explore a possible association with pesticide exposure (ie, the broad classes of insecticides, fungicides, and herbicides), using a job-exposure matrix.

Participants and methods

This study was one component of a large population-based case-control study of multiple myeloma and cancers of the esophagus, pancreas, and prostate. The persons forming the cases for the study consisted of black and white residents of Atlanta (DeKalb and Fulton counties), Detroit (Macomb, Oakland and Wayne counties), and New Jersey (10 counties), areas covered by population-based cancer registers. Eligible cases, those aged 30 to 79 years with multiple myeloma newly diagnosed between 1 August 1986 and 30 April 1989, were identified from pathology, hematology, outpatient, and tumor registry records. Because of the poor prognosis of multiple myeloma, a rapid-reporting system was developed to identify and interview cases within 3 months of diagnosis.

Population controls were selected from the same geographic areas and in the same time period as the cases and were proportional to the expected race, gender, and age distribution of the cases for the four cancer sites combined. Control participants under 65 years of age were selected by random digit dialing (RDD), using a two-step selection process involving the identification of eligible households followed by the selection of eligible persons (9). Control participants aged 65 to 79 years were randomly selected from rosters of Medicare recipients provided for each study area by the Health Care Financing Administration (HCFA) with stratification by age, gender, and race.

Most of the participants were interviewed in person at home. The control participants were interviewed in the same time period as the case participants. Detailed information was obtained on sociodemographic factors, occupation, history of living or working on a farm, dietary factors, smoking, and medical history. Information on occupation and industry were coded according to the standard occupational classification (SOC) systems (10) and the standard industrial classification (SIC) (11). For women, only the usual occupation was obtained and coded. The results are presented for all SOC 2-digit occupational groups and for SOC 3-digit and SOC-4 digit occupations with elevated risks in this or other investigations.

To assess occupational exposure to the three major classes of pesticides (ie, insecticides, fungicides, and herbicides), we used a job-exposure matrix developed by an industrial hygienist (PAS). The matrix was based on an extensive review of the literature to identify pesticide use and the exposure levels. On the basis of this review, the level (0=unexposed, 1=low, 2–4=moderate or high) and probability (0=unexposed, 1=low, 2–4=moderate to high) of exposure to each of the three pesticide classes was assigned for the occupation and industry combination of each participant. Selected occupations are shown in table 1 as examples of the scoring of the job-exposure matrix.

Odds ratios (OR) and 95% confidence intervals (95% CI) for the analyses of the ever–never occupational group, history of living on a farm, and pesticide exposure were estimated in a unconditional logistic regression analysis (12). Race-specific OR values were adjusted for age at diagnosis (cases) or interview (controls), gender, study area, and education. The overall OR values also included adjustment for race. A trend test for pesticide exposure level was performed by entering the exposure level into the logistic regression model as a continuous variable.

Table 1. Scores of the job- or industry-exposure matrix for industry or occupation combinations with a high probability of exposure to herbicides, insecticides, or fungicides. (– = unexposed or low probability of exposure regardless of exposure level)

Industry [a]	Job [b]	Herbicide level	Insecticide level	Fungicide level
Cotton (0131)	Crop, vegetable, fruit and nut farmers (5513)	High	High	–
Cotton (0131)	General farm workers (5612)	High	High	–
Cotton (0131)	Field crop and vegetable farm workers, manual (5613)	High	High	–
Tobacco (0132)	Field crop and vegetable farm workers, manual (5613)	–	High	–
Sugar crops (0133)	Field crop and vegetable farm workers, manual (5613)	High	–	–
Deciduous tree fruits (0175)	Orchard and vineyard and related workers, manual (5614)	High	High	High
General farms, primarily crop (0191)	General farmers (5512)	High	High	–
General farms, primarily crop (0191)	Crop, vegetable, fruit and tree nut farmers (5513)	High	High	–
General farms, primarily crop (0191)	Field crop and vegetable farm workers, manual (5613)	High	High	–
Lawn and garden services (0782)	Supervisors and related agricultural workers (5621)	Moderate	Moderate	–
Lawn and garden services (0782)	Groundskeepers and gardeners, except farm (5622)	Moderate	Moderate	–
Public golf courses (7992)	Supervisors and related agricultural workers (5621)	Moderate	–	Moderate

[a] Code of the Standard Industrial Classification in parentheses.
[b] Code of the Standard Occupational Classification in parentheses.

Of the 309 black and 581 white persons identified as possible case participants for the study, interviews were successfully conducted with 206 (66.7%) blacks (91 men and 115 women) and 367 (63.2%) whites (193 men and 174 women). The response rate was 67% for both the black and white RDD controls and 61% for the black and 57% for the white HCFA controls. The analyses were conducted using 967 black controls (614 men and 353 women), and 1164 white controls (742 men and 422 women). More detail on inclusion can be found in another paper by Baris et al (13).

Results

Odds ratios for multiple myeloma by occupation are presented in table 2. Significantly increased risks were observed for pharmacists, dieticians and therapists as a group (OR 6.10, 95% CI 1.65–22.5), service occupations (OR 1.30, 95% CI 1.02–1.65), roofers (OR 3.29, 95% CI 1.10–9.80), precision printing occupations (OR 10.1, 95% CI 1.03–99.50), heating equipment operators (OR 4.70, 95% CI 1.40–15.80), and hand molders and casters (OR 2.93, 95% CI 1.02–8.43). Twofold or greater risks of myeloma were found for timber cutting and related occupations (OR 2.28, 95% CI 0.55–9.54), plumbers, pipefitters and steam fitters (OR 2.11, 95% CI 0.71–6.23), lay-out workers (OR 4.48, 95% CI 0.95–21.10), sheet metal workers (OR 2.14, 95% CI 0.50–9.17), machine set-up operators (OR 2.17, 95% CI 0.56–8.38), press and break machine operators (OR 2.08, 95% CI 0.91–4.75), drilling and boring machine operators (OR 2.15, 95% CI 0.84–5.52), supervisors of handlers and equipment cleaners (OR 2.44, 95% CI 0.73–8.22), precision production helpers (OR 2.53, 95% CI 0.71–8.94), helpers of mechanics and repairers (OR 2.36, 95% CI 0.70–8.03), and parking lot attendants (OR 2.16, 95% CI 0.55–8.39), but these elevations were based on small numbers and none was statistically significant. The OR values for these occupations were similar for the blacks and whites.

Nonsignificantly increased myeloma risks were observed for farm operators and managers (OR 1.32, 95% CI 0.66–2.66), general farmers (OR 1.86, 95% CI 0.76–4.59), and general farm workers (OR 1.37, 95% CI 0.82–2.27), but not for crop, vegetable, fruit and tree nut farmers (OR 0.92, 95% CI 0.26–3.27) or field crop and vegetable farm workers (OR 0.62, 95% 0.24–1.62). For these farm-related occupations, the OR values for the blacks were similar in magnitude to those of the whites.

A detailed investigation of farm-related exposures is shown in table 3. Overall, the risk of myeloma was not increased for the participants who lived or worked on a farm or ranch as a teen or adult for a period of >6 months when compared with those who never lived or worked on a farm. The risk was slightly increased, however, for those who lived or worked on a farm for 20 or more years (OR 1.25, 95% CI 0.82–1.91). There was no increased risk for the participants who lived or worked on a farm and personally handled pesticides. The participants who lived or worked on a farm or ranch where sheep were raised had a significantly increased risk (OR 1.66, 95% CI 1.03–2.66) with excess risks for both the blacks (OR 1.76, 95% CI 0.81–3.82) and the whites (OR 1.62, 95% CI 0.88–2.98). Risks were higher for the men (OR 2.02, 95% CI 1.12–3.65) than the women (OR 1.27, 95% CI 0.60–2.83) (data not shown). These point estimates did not change after adjustment for exposure to other animals. There was no increased risk of myeloma for the participants who lived or worked on a farm or ranch where cattle, chickens, or pigs were raised.

Table 4 shows the risk of multiple myeloma in association with occupational exposure to any pesticide and to the three major classes of pesticides (insecticides, fungicides, and herbicides) assessed using the job-exposure matrix. All of the participants with a low probability of exposure were excluded from these analyses. For the blacks and whites combined, nonsignificantly increased risks were found with moderate or high occupational exposure to all pesticides (OR 1.25, 95% CI 0.89–1.75), herbicides (OR 1.48, 95% CI 0.72–3.04), insecticides (OR 1.60, 95% CI 0.79–3.25), and fungicides (OR 2.31, 95% CI 0.67–7.95). Black participants tended to have higher risks than white participants, but the number of exposed participants was small. After adjustment for the use of other pesticides, only the OR associated with insecticides declined, to 1.17 (95% CI 0.51–2.73) (data not shown). No significant exposure–response gradients were observed for pesticides as a whole or for herbicides, insecticides or fungicides separately. These analyses were repeated after the participants with a low probability of exposure were included. The point estimates, not shown, were lower.

Discussion

In this population-based study conducted in three areas of the United States, we found modestly increased risks of multiple myeloma for farm occupations and exposure to pesticides but significantly increased risks for living or working on a farm with sheep.

Employment in farm-related occupations has consistently been suggested as a risk factor for myeloma (6, 8, 14–21). The OR values of 1.32 (95% CI 0.66–2.66) for farm operators and managers, 1.37 (95% CI 0.82–2.27) for general farmers, and 1.86 (95% CI

Table 2. Odds ratios (OR) and 95% confidence intervals (95% CI) for multiple myeloma by occupation.[a]

Occupational title [b]	Cases	Controls	OR [c]	95% CI
Administrators (11,12,13)	24	177	0.70	0.40–1.10
Management related occupations (14)	23	112	1.01	0.62–1.63
Engineers, surveyors, architects (16)	12	59	0.99	0.51–1.90
Social, recreation and religious workers (20)	5	29	0.85	0.32–2.25
Teachers; college, university, postsecondary (22)	3	18	1.10	0.31–3.87
Teachers; except postsecondary institution (23)	22	98	1.03	0.62–1.70
Registered nurses (29)	4	22	0.49	0.16–1.46
Pharmacists, dietitians, therapists (30)	6	4	6.10	1.65–22.50
Writers, artists, performers (32)	4	41	0.46	0.16–1.31
Editors, reporters, public relations specialists (33)	4	10	1.89	0.56–6.36
Health technologists and technicians (36)	7	22	1.49	0.62–3.60
Licensed nurses (366)	3	8	1.53	0.39–5.97
Engineering and related technologists technicians (37)	7	43	0.76	0.33–1.73
Technicians; except health, engineering, science (39)	8	48	0.84	0.39–1.82
Supervisors; marketing and sales occupations (40)	15	81	0.78	0.44–1.38
Insurance, securities, real estate (41)	14	60	1.11	0.61–2.05
Sales, commodities except retail (42)	13	72	0.89	0.48–1.66
Sales, retail (43)	39	191	0.88	0.60–1.27
Sales related occupations (44)	4	30	0.67	0.23–1.96
Administrative support, including clerical (46)	49	221	0.83	0.59–1.17
Private household (50)	15	61	0.74	0.41–1.36
Protective service (51)	19	84	1.14	0.68–1.93
Service occupations (52)	125	447	1.30	1.02–1.65
Food and beverage preparation occupations (521)	57	202	1.27	0.92–1.76
Health service (523)	23	62	1.56	0.94–2.58
Cleaning and building service (524)	39	165	1.16	0.79–1.70
Janitors and cleaners (5244)	28	138	1.02	0.66–1.59
Personal service occupations (525–526)	8	24	1.53	0.67–3.49
Hairdressers cosmetologists (5253)	4	22	0.58	0.20–1.72
Farm operators and managers (55)	11	38	1.32	0.66–2.66
General farmers (5512)	7	18	1.86	0.76–4.59
Crop, vegetable, fruit and tree nut farmers (5513)	3	15	0.92	0.26–3.27
Other agricultural and related occupations (56)	35	180	0.92	0.62–1.37
General farm workers (5612)	22	73	1.37	0.82–2.27
Field crop and vegetable farm workers (hand) (5613)	5	41	0.62	0.24–1.62
Related agricultural occupations (562)	4	45	0.44	0.15–1.24
Groundskeepers gardeners, except farm (5622)	4	33	0.60	0.21–1.73
Forestry and logging occupations (57)	3	14	0.98	0.27–3.50
Timber cutting (573)	3	6	2.28	0.55–9.54
Supervisors; mechanics and repairers (60)	3	29	0.44	0.13–1.45
Mechanics and repairers (61)	40	216	0.81	0.56–1.18
Bus and truck engine diesel engine mechanics (6112)	6	19	1.34	0.53–3.43
Aircraft mechanics (6116)	7	17	1.89	0.77–4.68
Supervisors; construction and extractive occupations (63)	8	24	1.50	0.65–3.42
Construction trades (64)	46	167	1.30	0.91–1.88
Carpenters and related workers (642)	10	34	1.15	0.55–2.40
Electricians and power transmission installers (643)	5	12	1.86	0.64–5.46
Painters, paperhangers, plasterers (644)	10	32	1.33	0.63–2.77
Plumbers, pipefitters steamfitters (645)	5	11	2.11	0.71–6.23
Other construction trades (646–647)				
Roofers (6468)	6	8	3.29	1.10–9.80

(continued)

Table 2. Continued.

Occupational title [b]	Cases	Controls	OR [c]	95% CI
Supervisors; precision production occupations (67)	4	17	1.17	0.38–3.59
Precision production occupations (68)	45	158	1.13	0.79–1.61
Tool and die makers (6811)	7	19	1.35	0.55–3.27
Machinists (6813)	5	18	1.16	0.42–3.20
Precision metal workers (682)	7	17	1.73	0.70–4.28
Lay-out workers (6821)	3	4	4.48	0.95–21.10
Sheet metal workers (6824)	3	5	2.14	0.50–9.17
Precision printing (682)	3	1	10.10	1.03–99.50
Precision workers, assorted materials (686)				
Precision electrical electronic equipment (6867)	3	12	0.78	0.22–2.82
Butchers and meat cutters (6871)	4	16	1.06	0.35–3.25
Plant and system operators (69)	3	13	1.03	0.29–3.73
Supervisors; production occupations (71)	17	67	1.12	0.64–1.95
Machine setup operators (73)	5	24	0.79	0.30–2.13
Metal working and plastic working machine setup (731)	3	15	0.72	0.21–2.55
Machine setup operators (74)	3	8	2.17	0.56–8.38
Machine operators and tenders (75)	48	151	1.34	0.94–1.91
Metalworking and plastic working machine operators and (751)	25	76	1.38	0.85–2.23
Press and brake machine (7517)	9	20	2.08	0.91–4.75
Drilling and boring machine (7518)	7	13	2.15	0.84–5.52
Metalworking and plastic working machine operators (752)	11	55	0.81	0.42–1.59
Metal fabricating machine (753)	4	7	1.99	0.56–7.11
Metal and plastic processing machine operators and tend (754)	12	34	1.56	0.79–3.10
Molding and casting machine (7542)	3	17	0.76	0.22–2.64
Heating equipment (7544)	6	5	4.70	1.40–15.80
Machine operators and tenders (76)	59	244	0.90	0.65–1.23
Woodworking machine (763)	4	26	0.75	0.26–2.19
Printing machine (764)	3	24	0.53	0.16–1.80
Fabricators, assemblers, and hand working occupations (77)	59	227	1.17	0.85–1.63
Welders and solderers (771)	10	57	0.82	0.41–1.63
Hand working occupations (775)				
Hand molding and casting (7754)	6	9	2.93	1.02–8.43
Hand grinding polishing (7758)	3	9	1.37	0.36–5.23
Production inspectors, testers, samplers weighers (78)	20	55	1.41	0.82–2.40
Supervisors; transportation and material moving (81)	3	10	1.67	0.45–6.22
Transportation occupations (82)	60	304	0.94	0.69–1.30
Truck drivers, tractor-trailer (8212)	3	24	0.61	0.18–2.07
Truck drivers, heavy (8213)	29	155	0.89	0.58–1.37
Truck drivers, light (8214)	13	68	0.92	0.50–1.71
Material moving (83)	19	99	0.90	0.54–1.52
Supervisors; handlers, equipment cleaners, helpers (85)	4	9	2.44	0.73–8.22
Helpers (86)	12	51	1.15	0.60–2.20
Helpers; precision production (8619)	4	7	2.53	0.71–8.94
Helpers; mechanics and repairers (861)	4	8	2.36	0.70–8.03
Handlers, equipment cleaners and laborers (87)	72	410	0.80	0.60–1.08
Construction laborers (871)	17	110	0.73	0.42–1.24
Parking lot attendants (874)	3	8	2.16	0.55–8.39
Military (91)	37	165	1.05	0.71–1.55
Miscellaneous occupation s (99)	76	170	1.11	0.81–1.54

[a] OR values are included for all SOC 2-digit occupations and for selected SOC 3- and SOC 4-digit occupations either with an a priori hypothesis from the literature or with a statistically significant finding in our study.
[b] Standard occupational classification code in parentheses.
[c] OR values have been adjusted for gender, race, state of residence, and education.

Table 3. Odds ratios (OR) and 95% confidence intervals (CI) for multiple myeloma and farm exposure by race.

Exposure	Total				Blacks				Whites			
	Cases	Controls	OR[a]	95% CI	Cases	Controls	OR[b]	95% CI	Cases	Controls	OR[b]	95% CI
Lived or worked on a farm												
No	432	1550	1.00	·	141	606	1.00	·	291	944	1.00	·
Yes	136	569	0.91	0.72–1.15	65	359	0.80	0.57–1.13	71	210	1.11	0.81–1.53
Years lived or worked on a farm												
<5 years	28	108	1.02	0.65–1.58	13	69	0.88	0.47–1.67	15	39	1.24	0.65–700
5–9 years	38	155	0.95	0.64–1.39	17	95	0.82	0.47–1.44	21	60	1.21	0.66–2.35
10–19 years	35	209	0.66	0.44–0.97	20	138	0.62	0.36–1.04	15	71	0.75	0.41–1.36
≥20 years	35	95	1.25	0.82–1.91	15	55	1.19	0.63–2.24	20	40	1.41	0.79–2.52
Lived or worked on a farm and personally handled pesticides or herbicides												
Pesticides	17	106	0.77	0.45–1.32	10	59	0.96	0.47–1.98	7	47	0.60	0.25–1/34
Herbicides	8	44	0.86	0.40–1.87	6	23	1.58	0.61–4.05	2	21	0.35	0.08–1.54
Any	20	109	0.88	0.53–1.47	12	62	1.12	0.57–2.19	8	47	0.66	0.30–1.36
Livestock on farm												
Dairy cattle												
No	16	88	0.73	0.42–1.28	4	53	0.35	0.12–1.01	12	35	1.18	0.59–2.37
Yes	117	455	0.97	0.75–1.24	60	290	0.91	0.64–1.30	57	165	1.14	0.80–1.63
Beef cattle												
No	74	261	1.04	0.78–1.40	31	154	0.87	0.55–1.36	43	107	1.28	0.86–1.91
Yes	58	282	0.80	0.58–1.11	33	189	0.79	0.51–1.22	25	93	0.95	0.58–1.55
Pigs												
No	12	76	0.60	0.32–1.13	4	30	0.63	0.21–1.84	8	46	0.58	0.26–1.26
Yes	120	467	0.99	0.77–1.26	60	313	0.84	0.59–1.20	60	154	1.33	0.93–1.89
Sheep												
No	103	485	0.82	0.64–1.06	54	317	0.75	0.52–1.08	49	168	1.02	0.71–1.48
Yes	29	58	1.66	1.03–2.66	10	26	1.76	0.81–3.82	19	32	1.62	0.88–2.98
Chickens												
No	10	40	0.96	0.47–1.97	2	21	0.42	0.96–1.87	8	19	1.38	0.58–3.30
Yes	122	503	0.92	0.72–1.17	62	322	0.85	0.60–1.21	60	181	1.11	0.79–1.57

[a] OR values have been adjusted for age, gender, race, state of residence, and education.
[b] OR values have been adjusted for age, gender, state of residence, and education.

Table 4. Odds ratios (OR) and 95% confidence intervals (95% CI) for multiple myeloma and pesticide exposure by race.[a]

Exposure	Total				Blacks				Whites			
	Cases	Controls	OR[b]	95% CI	Cases	Controls	OR[c]	95% CI	Cases	Controls	OR[c]	95% CI
Pesticides												
None	360	1382	1.00	·	104	538	1.00	·	256	844	1.00	·
Low	151	545	1.13	0.90–1.41	76	323	1.09	0.77–1.54	75	222	1.07	0.78–1.46
Moderate or high	57	181	1.25	0.89–1.75	25	103	1.22	0.73–2.02	32	78	1.22	0.77–1.94
Test for trend			P=0.14				P=0.43				P=0.39	
Herbicides												
None	511	1920	1.00	·	174	835	1.00	·	337	1085	1.00	·
Low	15	39	1.45	0.78–2.69	8	21	1.58	0.67–3.72	7	18	1.24	0.50–3.10
Moderate or high	11	29	1.48	0.72–3.04	5	15	1.69	0.59–4.87	6	14	1.19	0.44–3.23
Test for trend			P=0.18				P=0.22				P=0.64	
Insecticides												
None	439	1664	1.00	·	133	667	1.00	·	306	997	1.00	·
Low	46	201	0.82	0.57–1.18	31	154	0.72	0.46–1.15	15	47	0.89	0.48–1.65
Moderate or high	12	28	1.60	0.79–3.25	6	16	1.74	0.65–4.71	6	12	1.39	0.50–3.86
Test for trend			P=0.79				P=0.84				P=0.76	
Fungicides												
None	406	1558	1.00	·	125	645	1.00	·	281	913	1.00	·
Low	145	487	1.15	0.91–1.44	70	84	1.10	0.79–1.55	75	203	1.08	0.79–1.45
Moderate or high	4	8	2.31	0.67–7.95	2	4	2.91	0.51–16.70	2	4	1.55	0.27–8.90
Test for trend			P=0.14				P=0.39				P=0.54	

[a] All participants with low probability have been excluded.
[b] OR values have been adjusted for age, gender, race, state of residence, and education.
[c] OR values have been adjusted for age, gender, state of residence, and education.

0.76–4.59) for general farm workers in our study are similar in magnitude to the OR of 1.38 (95% CI 1.27–1.51) reported in a meta-analysis of 32 studies published between 1981 and 1996 (5). Although the specific exposures responsible for the association between myeloma and farming are not known, suspected agents are pesticides (21, 22), engine exhaust (23, 24), grain dust (25), and animal viruses (15).

The participants who lived and worked on a farm as a teen or adult and had personally handled herbicides did not show an increased risk of myeloma. This absence of an association may be related to the possibility of lower exposure to pesticides among those who lived or worked on a farm than that of those who reported farming as their occupation.

For the participants with moderate or high occupational exposure to pesticides, our OR of 1.25 (95% CI 0.89–1.75) is consistent with the risks reported in Danish case-control studies of men (OR 1.2, 95% CI 0.7–1.9) (26) and women (OR 1.3, 95% CI 0.8–2.1) (27), as well as with the findings of other studies that showed an increased risk of myeloma from pesticide exposure (6, 20, 28–30). Our estimates of risk by specific type of exposure revealed that excess risk was mainly associated with herbicide and fungicide exposure. In a cohort study of Dutch-licensed applicators who only applied herbicides, myeloma mortality was elevated by a factor of 8.2 (95% CI 1.6–23) when compared with the general population (31). Dioxin (2,3,8-tetrachlorodibenzo-p-dioxin) has been a chemical contaminant in some commonly used herbicides and has been associated with myeloma risk (32).

The excess risk of myeloma from occupational pesticide exposure is consistent with the immunotoxic effects of pesticides observed for both animals (33) and humans (34, 35). Some herbicides have been shown to impair cytokine production (36, 37) and induce immunosupression (38). Immunologic clues on the etiology of myeloma are also provided by studies showing an excess risk for patients with autoimmune diseases and with certain conditions associated with chronic antigen stimulation (3).

Our finding of an excess risk for participants who lived or worked on a farm where sheep were raised is consistent with the findings of a previous study (15). Excesses have also been found for workers in cattle, sheep, or pig slaughterhouses (39) and for workers exposed to sheep (6). Although contact with other animals was not associated with an increased risk of myeloma in our study, excess risks have been found in other investigations (6, 15, 39). Exposure to animal viruses through contact with farm animals may be involved in myeloma risk (15), although no specific agent has been identified. Sheep workers may be exposed to parapoxvirus orf virus, which causes an acute contagious skin disease in humans, particularly among sheep farmers, animal handlers, and meat workers (40). Interestingly, the orf virus encodes a homolog of interleukin-10 (41, 42), one of the most important cytokines regulating the proliferation and cellular characteristics of myeloma cells (43).

We found elevated OR values for several occupations that had been previously reported, such as timber cutting and related occupations (20), plumbers, pipefitters and steamfitters (17, 20), painters (20, 44, 45), food and beverage preparation workers (17), health and science technicians (46), and janitors and cleaners (47). Our finding of an increased risk of myeloma for several metal work-related occupations is consistent with the results of several other studies (30, 47–52). There is only limited information about exposure to specific metals and multiple myeloma. In general, metal workers are involved in a wide range of activities, ranging from fabricating, fitting and assembling metal components to shaping, planning and producing precision parts, and are exposed to a wide range of chemicals, including cutting oils and solvents, that may have carcinogenic effects. In our study, myeloma risk was not elevated for some of the occupations that a priori were of interest (eg, truck drivers, welders, and hairdressers and cosmetologists) (6, 24, 49, 53, 54).

Despite the large size of our study, we had small numbers of exposed participants and limited power to examine risks for specific occupations. The job-exposure matrix for pesticides was based on the participants' most common occupation rather than on their entire occupational history; therefore, misclassification may have occurred. Lack of information on the start and end date of the most common occupation may have affected the accuracy of the exposure assignment for a given job, since we could not incorporate the changes in exposure over time. The misclassification related to the exposure assessment is probably nondifferential, tending to bias the results towards the null. In addition, we examined a large number of potential associations, and some, by chance alone, may have appeared to be elevated or depressed. For this reason, we focused on occupations that were suspected to be associated with an elevated risk of multiple myeloma.

There are several strengths of our study. Since the job-exposure matrix was developed for our study in particular, it reflects occupational exposures to pesticides more specifically for our cases and controls. This is not a typical situation for case-control studies of occupation and cancer, in which the investigators rely most of the time on a job-exposure matrix developed for general use or for another study. The large number of cases and controls made it possible to examine the risk of myeloma by detailed occupational categories. Unlike many other studies of multiple myeloma, occupational data were obtained from the participants in personal interviews rather than from the next of kin. This procedure increased the accuracy of the information.

In conclusion, our study suggests a modest increased risk of multiple myeloma for occupational exposure to pesticides determined on the basis of a job-exposure matrix, but not for self-reported pesticide use. The observed increased risk for the participants who lived or worked on a farm where sheep were raised suggests that certain animal viruses may be involved in myeloma risk.

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